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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,293	09/23/2004	Liangzhi Xie	21038P	3707

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EXAMINER

CHEN, STACY BROWN

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1648

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/509,293	Applicant(s) XIE ET AL.	
	Examiner Stacy B. Chen	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 September 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/30/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment and response filed April 30, 2007 is acknowledged and entered.

Claims 5-15 are pending and under examination.

2. The rejection of claims 1-4 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing adenoviruses using the claimed method, does not reasonably provide enablement for the production of any type of virus, is moot in view of the cancellation of claims 1-4. The rejection does not apply to claims 5-15 because those claims are limited to the embodiment of adenoviruses.

Claims Summary

3. The claims are drawn to a method of producing adenovirus, comprising the following steps:

a) culturing host cells at a temperature below a physiological optimum for promoting host cell growth;

b) infecting the host cells with adenovirus;

c) culturing the adenovirus-infected host cells at or near a physiologically optimum temperature for producing adenovirus, wherein the culture temperature is above the culture temperature in step a);

d) harvesting adenovirus and/or cells containing adenovirus from the culture; and,

e) purifying adenovirus away from host cell and culture contaminants.

In another embodiment, the temperature of the host cell culture of step a) is initially at or near a temperature near a physiological optimum for host cell growth, then shifted to a

Art Unit: 1648

temperature below a physiological optimum for host cell growth prior to infecting the host cells with a virus. The culture temperature is lowered to a sub-optimal level for at least about 24 hours prior to infecting the host cells with the virus. In another embodiment, the culture temperature is lowered to a sub-optimal level for up to the entire cell passages prior to infecting the host cells with the virus. Specifically, the temperature for cell growth at the initial temperature in step a) is from 35°C to 38°C. The temperature is then shifted in step b) to a temperature from 31°C to 34°C. The temperature for growth of infected cells is from about 36°C to 38°C.

4. ***The rejection of claims 5-11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention, is maintained. The rejection of claims 12-15 under 35 U.S.C. 112, second paragraph, is withdrawn in view of Applicant's amendment.***

The metes and bounds of claims 1-8, with respect to the phrases, “at a temperature below a physiological optimum for host cell growth”, and, “at or near a physiologically optimum temperature for producing virus”, cannot be determined. It remains unclear what temperatures are encompassed by the phrases, “at a temperature below a physiological optimum for host cell growth”, and, “at or near a physiologically optimum temperature for producing virus”. While the physiological optimum may be generally 37°C, it is unclear what temperatures are encompassed when the temperatures are “below” 37°C, for example. Similarly, it is unclear what temperatures are encompassed when the temperatures are “near” 37°C, for example. Therefore, even if the optimal temperature is known to be 37°C, the temperatures below and near

Art Unit: 1648

37°C are not so clearly defined such that one of skill in the art would be able to determine what temperatures are encompassed by the claims.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

Applicant points out that the specification notes that the physiological temperature of 37°C has been shown to be optimal for growth of a majority of mammalian cell lines, and that a return to the physiological temperature depends on the respective host cell and/or virus.

Applicant asserts that it would be routine experimentation to determine the physiologically optimum temperature for the growth of a particular cell line and/or virus. Applicant asserts that the metes and bounds can readily be determined by the skilled artisan for any combination of virus and host cell. Applicant notes that the invention is based on the counter intuitive approach of reducing the cell culture temperature to a sub-optimal level and then shifting up to or near the physiological temperature for production.

In response to Applicant's arguments, the Office notes that the claims are limited to adenovirus production using the sub-optimal temperature method of the instant invention. Because the counter intuitive approach to culturing at optimal temperatures and then shifting to sub-optimal temperatures is novel for adenovirus production, the temperatures encompassed by the claim language should be sufficiently clear such that the metes and bounds of those temperatures are clearly understood. Applicant has provided a sub-optimal range of 31°C to 34°C, and an optimal range of from about 36°C to 38°C. These temperatures are sufficiently clear, as independent claims 12-15. However, the recitations of generally "below a physiological optimum temperature" and "near a physiologically optimum temperature" do not clearly convey

Art Unit: 1648

the inventive concept such that one would understand the limits of those temperature descriptions.

Applicant submits that the claims sufficiently apprise one of ordinary skill in the art of their scope and provide clear warning to others as to what constitutes infringement of the patent. In response, the Office does not consider the specification or the claim language as clearly conveying what constitutes infringement because the language is not limited to a clear definition. Even given the guidance in the specification, what constitutes “below a physiological optimum temperature” and “near a physiologically optimum temperature” is subject to individual interpretation and thus the claims do not clearly set forth the metes and bounds of the method steps. Therefore, the rejection is maintained for reasons of record.

Conclusion

5. Claims 12-15 are objected to for depending from rejected claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

Art Unit: 1648

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 7-30-2007
Primary Examiner, TC1600